

Cross-Canada differences in early-stage breast cancer treatment and acute-care use

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ABSTRACT

Background Chemotherapy has improved outcomes in early-stage breast cancer, but treatment practices vary, and use of acute care is common. We conducted a pan-Canadian study to describe treatment differences and the incidence of emergency department visits (EDVs), EDVs leading to hospitalization (EDVHS), and direct hospitalizations (HS) during adjuvant chemotherapy.

Methods The cohort consisted of women diagnosed with early-stage breast cancer (stages I–III) during 2007–2012 in British Columbia, Manitoba, Ontario, or Nova Scotia who underwent curative surgery. Parallel provincial analyses were undertaken using linked clinical, registry, and administrative databases. The incidences of EDVs, EDVHS, and HS in the 6 months after treatment initiation were examined for patients treated with adjuvant chemotherapy.

Results The cohort consisted of 50,224 patients. The proportion of patients who received chemotherapy varied by province, with Ontario having the highest proportion (46.4%), and Nova Scotia, the lowest proportion (38.0%). Age, stage, receptor status, comorbidities, and geographic location were associated with receipt of chemotherapy in all provinces. Ontario had the highest proportion of patients experiencing an EDV (36.1%), but the lowest proportion experiencing HS (6.4%). Conversely, British Columbia had the lowest proportion of patients experiencing an EDV (16.0%), but the highest proportion experiencing HS (26.7%). The proportion of patients having an EDVHS was similar across provinces (13.9%–16.8%). Geographic location was associated with EDVs, EDVHS, and HS in all provinces.

Conclusions Intra- and inter-provincial differences in the use of chemotherapy and acute care were observed. Understanding variations in care can help to identify gaps and opportunities for improvement and shared learnings.

Key Words Breast cancer, systemic therapy, administrative data, hospitalizations, emergency department visits

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INTRODUCTION

Breast cancer (BCa) is the most common cancer in Canadian women, accounting for approximately 25% of new cancer cases annually and approximately 13% of cancer-related deaths in women¹. Many women diagnosed with BCa will require some form of systemic treatment in either the adjuvant or metastatic setting. In the adjuvant setting, chemotherapy is recommended for lymph node–positive and triple-negative disease regardless of nodal status, where it is associated with a significant improvement

in survival compared with surgery alone^{2–5}. Despite the survival benefit, previous studies have noted variation in chemotherapy delivery and in the clinical characteristics of the patients who receive it^{6,7}.

Receipt of adjuvant chemotherapy therapy has been associated with a higher incidence of acute care use by treated women than by age-matched controls or clinical trial populations^{8,9}. A study by Hassett *et al.*¹⁰, examining rates of acute-care use in U.S. patients with newly diagnosed BCa, found that, compared with women who did not receive chemotherapy, women treated with chemotherapy

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were more likely to experience hospitalization (H) or an emergency department visit (EDV) for any cause (61% vs. 42%). A recent population-based study in Ontario assessed the frequency of EDVs and HS in women treated with adjuvant chemotherapy for early-stage bca compared with age- and comorbidity-matched non-cancer control participants⁸. Experience of EDVs and HS were significantly more common in patients with bca than in non-cancer control participants, with nearly half the patients experiencing at least 1 acute-care visit during the treatment period (43% vs. 9.3%, $p < 0.001$). In the cohort with bca, approximately 75% of the visits were considered to be treatment-related, with the most common reasons being fever, neutropenia, infection, or gastrointestinal symptoms. In multivariable analysis, patients receiving chemotherapy regimens that included docetaxel and patients with coexisting comorbidities had an increased risk of an acute-care visit. Substantial intraprovincial regional variation was evident in the rates: 30%–65% of patients (regions with the lowest and highest rates respectively) had at least 1 EDV or H (or both). Whether those findings are similar for other Canadian provinces is not known, but high rates of acute-care use by cancer patients have also been reported in other countries¹¹ and have a significant effect on quality of life and health care costs¹².

To evaluate intra- and interprovincial differences in the proportion and characteristics of patients receiving adjuvant chemotherapy for early-stage bca, we conducted, as part of the CANIMPACT study, parallel population-based analyses for 4 Canadian provinces: British Columbia, Manitoba, Ontario, and Nova Scotia¹³. For patients who received adjuvant chemotherapy, we also evaluated the proportions and characteristics of patients who experienced an EDV, an EDV leading to hospital admission (EDVH), or direct H during the first 6 months after initiation of treatment.

METHODS

Study Overview

The Canadian universal health care system consists of 13 public systems. The present work was undertaken as part of a large pan-Canadian study of bca care. That study used linked clinical, registry, and administrative data from British Columbia, Manitoba, Ontario, and Nova Scotia. The study was approved by all relevant research ethics boards, data access committees, and privacy committees. Data linkage and analyses were carried out in parallel in each of the participating provinces. A detailed description of the data sources and linkages was previously published¹³.

Cohort Creation and Explanatory Variable Definitions

The cohorts consisted of women newly diagnosed with stages I–III bca who underwent surgery with curative intent. The year of diagnosis for the patients varied by province because of data availability (British Columbia and Ontario: 2007–2010; Manitoba and Nova Scotia: 2007–2012). Women were excluded if they lacked a unique health identifier, had ductal carcinoma *in situ* or stage 0 disease, were non-residents of the province where they were treated, or had a previous history of cancer (with the exception of basal cell carcinoma). Of the 65,878 women newly diagnosed with stages I–III bca, 50,224 (76%) underwent surgery. Of the

patients included in the treatment analysis, 19,775 (39%) received adjuvant chemotherapy.

Based on census data, the “deprivation index” provides information about the distribution of material and social inequality across Canada. To allow for interprovincial comparisons, deprivation index quintiles were evaluated using the countrywide distribution as a reference; deprivation quintiles were not reported for the British Columbia cohort because the geocodes required to create the deprivation index were unavailable.

Comorbidities were evaluated using the Johns Hopkins (Baltimore, MD, U.S.A.) Aggregated Diagnosis Groups (ADGs)¹⁴. A high comorbidity burden was defined as 10 or more ADGs. The effect of geographic location of treatment was evaluated by health authority, whereby regional health authorities are responsible for the delivery of cancer care in a region of a province. The number of health authorities varied by province. Mastectomy and lumpectomy within the 2 weeks before, and up to 9 months after, the date of diagnosis were determined using procedure codes from hospitalization and physician billing data for Manitoba, Ontario, and Nova Scotia, and from cancer registry data in British Columbia¹⁵. Delivery of radiotherapy within 9 months of diagnosis was determined from cancer registries and scheduling databases.

Receipt of Chemotherapy

Delivery of chemotherapy was identified using procedure codes for the administration of intravenous chemotherapy within physician billing and claims data (Manitoba, Ontario, and Nova Scotia), provincial cancer pharmacy data (British Columbia), and patterns of visits to medical oncology in physician billings data and data from the cancer centre scheduling database (Nova Scotia). Patients were categorized as having received neoadjuvant chemotherapy if they had at least 1 record of chemotherapy before definitive surgery, and adjuvant chemotherapy if they received no chemotherapy before surgery but had at least 1 record of chemotherapy within 6 months after surgery. If no chemotherapy record was present, then the patient was categorized as having had surgery only. Associations between patient characteristics and receipt of adjuvant chemotherapy were evaluated by province.

Outcomes Assessment

For patients who received adjuvant chemotherapy, the incidences of all-cause, cancer- or treatment-related, and febrile neutropenia-related EDVs, EDVHS, and HS were evaluated for the 6-month period after the first chemotherapy administration. For HS, relevant incidences were identified in the Discharge Abstract Database maintained by the Canadian Institute for Health Information and were classified as either an EDVH or H based on “method of entry” variable in that database. Although EDVs could be identified using the National Ambulatory Care Reporting System (NACRS), those data were, for some provinces, either unavailable (British Columbia) or very limited (Nova Scotia). As a result, EDVs were identified from physician billing data by obtaining all claims for which the location of service was the emergency department and for which the date of service was not within 24 hours of H. Visits were then classified

as cancer-related [if the primary diagnostic code was bca (C50)] or as treatment-related (if the primary diagnostic code was a common toxicity of chemotherapy). The list of common toxicities, validated in previous studies^{8,16}, was based on *a priori* knowledge of chemotherapy toxicities, an independent review of diagnostic codes (*International Statistical Classification of Diseases and Related Health Problems*, 10th revision), and on algorithms used by Hassett *et al.*¹⁰. Visits were classified as being related to febrile neutropenia if the main diagnosis code was “neutropenia” (also based on a previously validated algorithm)¹⁶.

Statistical Analysis

Demographic and clinical characteristics and use of health care services are summarized by province using descriptive statistics. For patients who received adjuvant chemotherapy, the proportion of patients with at least 1 all-cause, cancer- or chemotherapy-related, or febrile neutropenia-related EDV, EDVH, or H were calculated. Associations of demographic, clinical, and health care characteristics with having received adjuvant chemotherapy or experienced an EDV or H were evaluated using the chi-square test; *p* values less than 0.05 were considered significant. All database manipulations and statistical analyses were performed using the SAS software application (version 9.3: SAS Institute, Cary, NC, U.S.A.).

RESULTS

Cohort Description

The cohort consisted of 11,701 patients from British Columbia, 3,736 from Manitoba, 31,575 from Ontario, and 3,212 from Nova Scotia. Table 1 summarizes the demographic and clinical characteristics of the cohort. Median age (60–61 years) and stage distribution were similar across the provinces, with most patients having stage 1 disease (44.2%–49.8%). The proportion of patients with unknown receptor status (estrogen, progesterone, or HER2) was high (45.9%–63.8%), except in Manitoba (6.3%). Compared with other provinces, Nova Scotia had a greater proportion of patients who were found to be in the most deprived quintile of the deprivation index (33.6% vs. 12.4%–17.9%). The greatest proportion of patients with a high comorbidity burden (10 or more ADGs) was also observed in Nova Scotia (20.4% vs. 10.7%–16.9%), and the greatest proportion of patients with a low comorbidity burden (0–3 ADGs) was observed in British Columbia (30.8% vs. 20.3%–24.9%). Compared with British Columbia and Ontario, Nova Scotia and Manitoba had a greater proportion of patients who resided in rural communities (34.5% and 28.8% vs. 12.8% and 12.6% respectively).

Treatment Patterns

In all analyzed provinces, a similar proportion of patients underwent lumpectomy (67.2%–71.2%); however, mastectomy was more common in Nova Scotia than in the other provinces (51.7% vs. 33.3%–36.9%). Radiotherapy was more commonly used in British Columbia and Ontario than in Manitoba or Nova Scotia (70.3% and 64.0% vs. 56.3% and 55.2% respectively). The proportion of patients who received adjuvant or neoadjuvant chemotherapy varied by province: 35.3%–40.7% for adjuvant chemotherapy, and 2.5%–5.7% for neoadjuvant chemotherapy. Patients treated

in Ontario were most likely to receive any chemotherapy (46.4%); patients treated in Nova Scotia were least likely to receive chemotherapy (38.0%).

Inter- and Intraprovincial Differences in Receipt of Chemotherapy

In all participating provinces, use of chemotherapy was associated with age, stage, receptor status, comorbidities, and geographic location (Table II). Younger patients and those with higher-stage disease, triple-negative receptor status, and lower comorbidity burden were more likely to receive chemotherapy in all provinces. Higher income was associated with receipt of chemotherapy in all provinces, except for Nova Scotia (*p* = 0.29). Deprivation index was significantly associated with receipt of chemotherapy in Manitoba (*p* = 0.02) and Ontario (*p* < 0.01), but not in Nova Scotia (*p* = 0.07). Patients in the most deprived quintile of the deprivation index were treated in greater proportion with surgery only rather than with the addition of adjuvant chemotherapy (Manitoba: 19.0% vs. 16.3%; Ontario: 13.1% vs. 11.6%; Nova Scotia: 35.5% vs. 31.1%). Conversely, a greater proportion of patients in the least deprived quintile received treatment with adjuvant chemotherapy rather than with surgery only (Manitoba: 22.0% vs. 18.7%; Ontario: 27.3% vs. 25.3%; Nova Scotia: 14.7% vs. 13.5%). Rurality was associated with chemotherapy use only in Nova Scotia (*p* < 0.01).

Inter- and Intraprovincial Differences in Acute-Care Use

The proportion of patients experiencing at least 1 EDVH was similar across provinces [13.9%–16.8%, Figure 1(A)]. Ontario had the highest proportion of patients with at least 1 all-cause EDV (36.1%), but the lowest proportion with HS (6.4%). Conversely, the proportion of patients having all-cause EDVs was lowest in British Columbia (16.0%), and the proportion having HS was the highest (26.7%). A similar pattern was observed for cancer- or chemotherapy-related visits [Figure 1(B)]. The proportion of patients experiencing at least 1 EDV or H related to neutropenia [Figure 1(C)] was generally low and similar across provinces (EDV: 0%–1.6%; EDVH: 7.1%–10.1%; H: 0.6%–1.9%).

Age and deprivation index were associated with experiencing an EDV in Ontario, Manitoba, and Nova Scotia; comorbidities and geographic location (health authority) were associated with experiencing an EDV in all provinces (Table III). Income quintile was associated with EDVs in Ontario (*p* < 0.01) and Nova Scotia (*p* = 0.03), but was not significant in British Columbia or Manitoba. Comorbidities and geographic location were associated with experiencing an EDVH in all provinces except Nova Scotia (Table IV). Age and geographic location were associated with experiencing at least 1 H across all provinces (Table V). Deprivation index was associated with HS in Ontario (*p* < 0.01) and Nova Scotia (*p* = 0.01), but not in Manitoba (*p* = 0.07). Comorbidities and rurality were associated with HS in Manitoba only (*p* = 0.02, *p* < 0.01 respectively).

DISCUSSION

Parallel analyses undertaken in 4 Canadian provinces found statistically significant inter- and intraprovincial

TABLE I Cohort demographics and clinical characteristics

Characteristic	British Columbia	Manitoba	Ontario	Nova Scotia
Eligible patients	11,701	3,736	31,575	3,212
Age at diagnosis (years)				
Mean	60.9±13.0	62±13.7	60.4±13.4	61.3±13.2
Median	61	61	60	61
IQR	51–70	51–71	50–70	51–71
Stage [<i>n</i> (%)]				
I	5,824 (49.8)	1,674 (44.8)	13,960 (44.2)	1,583 (49.3)
II	4,329 (37.0)	1,514 (40.5)	12,995 (41.2)	1,201 (37.4)
III	1,548 (13.2)	548 (14.7)	4,620 (14.6)	428 (13.3)
Receptor status [<i>n</i> (%)]				
ER+ or PgR+, HER2+	2,380 (20.3)	349 (9.3)	1,357 (4.3)	169 (5.3)
ER+ or PgR+, HER2–	3,087 (26.4)	2,620 (70.1)	8,273 (26.2)	1,168 (36.4)
ER– and PgR–, HER2+	481 (4.1)	160 (4.3)	641 (2.0)	40 (1.3)
ER– and PgR–, HER2–	388 (3.3)	370 (9.9)	1,158 (3.7)	120 (3.7)
Unknown	5,365 (45.9)	237 (6.3)	20,146 (63.8)	1,715 (53.4)
Income quintile [<i>n</i> (%)]				
Q1 (lowest)	2,113 (18.1)	575 (15.4)	5,477 (17.3)	563 (17.5)
Q2	2,319 (19.8)	790 (21.2)	6,115 (19.4)	646 (20.1)
Q3	2,305 (19.7)	750 (20.1)	6,060 (19.2)	632 (19.7)
Q4	2,327 (19.9)	825 (22.1)	6,678 (21.1)	709 (22.1)
Q5 (highest)	2,503 (21.4)	789 (21.1)	7,138 (22.6)	654 (20.4)
Unknown	134 (1.1)	7 (0.2)	107 (0.3)	8 (0.3)
Deprivation index [<i>n</i> (%)]				
Q5 (most deprived)	NA	667 (17.9)	3,927 (12.4)	1,079 (33.6)
Q4	NA	770 (20.6)	5,170 (16.4)	680 (21.2)
Q3	NA	735 (19.7)	6,531 (20.7)	498 (15.5)
Q2	NA	685 (18.3)	7,296 (23.1)	478 (14.9)
Q1 (least deprived)	NA	747 (20.0)	8,273 (26.2)	448 (14.0)
Unknown	NA	132 (3.5)	378 (1.2)	29 (0.9)
Comorbidities [<i>n</i> (%)]				
0–3 ADGs	3,601 (30.8)	832 (22.3)	7,857 (24.9)	651 (20.3)
4–5 ADGs	2,956 (25.3)	866 (23.2)	7,248 (23.0)	673 (21.0)
6–7 ADGs	2,349 (20.1)	790 (21.2)	6,901 (21.9)	681 (21.2)
8–9 ADGs	1,547 (13.2)	615 (16.5)	4,891 (15.5)	551 (17.2)
≥10 ADGs	1,248 (10.7)	633 (16.9)	4,678 (14.8)	656 (20.4)
Health authority ^a [<i>n</i> (%)]				
1	2,202 (18.8)	405 (10.8)	1,791 (5.7)	208 (6.5)
2	3,885 (33.2)	114 (3.1)	2,532 (8.0)	201 (6.3)
3	2,728 (23.3)	507 (13.6)	1,739 (5.5)	295 (9.2)
4	2,392 (20.4)	469 (12.6)	3,829 (12.1)	269 (8.4)
5	452 (3.9)	2,241 (60.0)	1,163 (3.7)	78 (2.4)

TABLE I Continued

Characteristic	British Columbia	Manitoba	Ontario	Nova Scotia
Health authority ^a [n (%)] continued				
6	—	—	1,821 (5.8)	173 (5.4)
7	—	—	2,758 (8.7)	171 (5.3)
8	—	—	4,162 (13.2)	472 (14.7)
9	—	—	3,965 (12.6)	1,342 (41.8)
10	—	—	1,413 (4.5)	—
11	—	—	3,300 (10.5)	—
12	—	—	1,228 (3.9)	—
13	—	—	1,278 (4.0)	—
14	—	—	586 (1.9)	—
Unknown	42 (0.4)	—	10 (0.0)	^b
Residence [n (%)]				
Urban	10,189 (87.1)	2,653 (71.0)	27,593 (87.4)	2,100 (65.4)
Rural	1501 (12.8)	1075 (28.8)	3979 (12.6)	1108 (34.5)
Unknown	11 (0.1)	8 (0.2)	≤5	≤5
Treatment [n (%)]				
Lumpectomy	7,867 (67.2)	2,650 (70.9)	22,294 (70.6)	2,286 (71.2)
Mastectomy	3,893 (33.3)	1,350 (36.1)	11,663 (36.9)	1,661 (51.7)
Chemotherapy				
Adjuvant	4,319 (36.9)	1,472 (39.4)	12,851 (40.7)	1,133 (35.3)
Neoadjuvant	424 (3.6)	94 (2.5)	1,791 (5.7)	87 (2.7)
NOS	133 (1.1)	177 (4.7)	151 (0.5)	66 (2.1)
Radiotherapy	8,230 (70.3)	2,103 (56.3)	20,206 (64.0)	1,772 (55.2)

^a Used as a proxy for evaluating geographic variation. Number of health authorities vary by province.

^b Too few cases to report.

IQR = interquartile range; ER = estrogen receptor; PgR = progesterone receptor; HER2 = human epidermal growth factor receptor 2; NA = not available; ADGs = Aggregate Diagnosis Groups (Johns Hopkins, Baltimore, MD, U.S.A.); NOS = not otherwise specified.

differences in treatment and acute-care use during adjuvant chemotherapy for early-stage bca. Demographic and clinical factors such as age, comorbidity, and stage were associated with receipt of chemotherapy. Although rates of acute-care visits were high in all 4 provinces, differences in the types of visits were evident. To date, most of the Canadian literature evaluating acute-care use during chemotherapy has examined Ontario^{8,16–18}. Our study suggests that the findings in those studies might not directly translate to other provinces. Understanding aspects of local care delivery that drive differences in treatment and acute-care use will help to identify opportunities for learning and improvement.

Lumpectomy rates were similar across the participating provinces, but mastectomy was more common in Nova Scotia. The observed mastectomy rates are comparable to rates reported previously in a population-based study by Porter *et al.*¹⁹ evaluating surgical patterns across Canada. Radiotherapy was more commonly used in British Columbia and Ontario than in Manitoba or Nova Scotia. Patients

treated in Ontario were most likely to receive chemotherapy, either adjuvant or neoadjuvant; patients treated in Nova Scotia were least likely to receive chemotherapy. Those findings, coupled with the observed association between geographic location and receipt of chemotherapy, suggests that issues with access or availability might affect the use of some treatment modalities in some provinces, particularly those with less population density or greater travel distances to the nearest cancer facility (such as Manitoba or Nova Scotia). Those findings are consistent with two previous studies in the United States that demonstrated an effect of distance to radiation therapy on the likelihood of a patient undergoing mastectomy^{20,21}. The observed association between increased age and decreased use of chemotherapy across all provinces is consistent with previous findings^{22–24} despite evidence that chemotherapy-related improvements in patient outcomes extend to older women. Stage and receptor status were associated with receipt of chemotherapy in all provinces, an observation similar to those in previous reports from China and the United States^{22,25} and

TABLE II Continued

Characteristic	Provincial group [n (%)]					
	British Columbia (n=11,144)		Manitoba (n=3,465)		Ontario (n=29,633)	
	Adjuvant chemotherapy	p Value	Adjuvant chemotherapy	p Value	Adjuvant chemotherapy	p Value
	Yes No		Yes No		Yes No	
	(n=4,319, 38.8%)	(n=6,825, 61.2%)	(n=1,472, 42.5%)	(n=1,993, 57.5%)	(n=12,851, 43.4%)	(n=16,782, 56.6%)
					Yes No	(n=1,133, 37.6%) (n=1,884, 62.4%)
						p Value
Deprivation index						
Q5 (most deprived)	NA	NA	240 (16.3)	379 (19.0)	1,484 (11.6)	2,200 (13.1)
Q4	NA	NA	281 (19.1)	437 (21.9)	1,985 (15.5)	2,868 (17.1)
Q3	NA	NA	277 (18.8)	398 (20.0)	2,685 (20.9)	3,461 (20.6)
Q2	N/A	N/A	297 (20.2)	338 (17.0)	3,061 (23.8)	3,790 (22.6)
Q1 (least deprived)	NA	NA	324 (22.0)	372 (18.7)	3,506 (27.3)	4,237 (25.3)
Unknown	NA	NA	53 (3.6)	69 (3.5)	130 (1.0)	226 (1.4)
Comorbidities						
0-3 ADGs	1,602 (37.1)	1,762 (25.8)	406 (27.6)	355 (17.8)	3,584 (27.9)	3,607 (21.5)
4-5 ADGs	1,143 (26.5)	1,682 (24.6)	346 (23.5)	442 (22.2)	3,126 (24.3)	3,636 (21.7)
6-7 ADGs	784 (18.2)	1,462 (21.4)	317 (21.5)	422 (21.2)	2,832 (22.0)	3,664 (21.8)
8-9 ADGs	488 (11.3)	1,001 (14.7)	204 (13.9)	366 (18.4)	1,831 (14.3)	2,840 (16.9)
≥10 ADGs	302 (7.0)	918 (13.5)	199 (13.5)	408 (20.5)	1,478 (11.5)	3,035 (18.1)
Health authority ^a						
1	802 (18.6)	1,305 (19.1)	158 (10.7)	219 (11.0)	713 (5.6)	983 (5.9)
2	1,524 (35.3)	2,142 (31.4)	57 (3.9)	46 (2.3)	1,005 (7.8)	1,329 (7.9)
3	960 (22.2)	1,610 (23.6)	157 (10.7)	312 (15.7)	660 (5.1)	965 (5.8)
4	787 (18.2)	1,546 (22.7)	179 (12.2)	250 (15.5)	1,474 (11.5)	2,107 (12.6)
5	229 (5.3)	197 (2.9)	921 (62.6)	1,166 (58.5)	543 (4.2)	522 (3.1)
6	—	—	—	—	756 (5.9)	969 (5.8)
7	—	—	—	—	1,071 (8.3)	1,476 (8.8)
8	—	—	—	—	1,790 (13.9)	2,120 (12.6)
9	—	—	—	—	1,714 (13.3)	2,061 (12.3)
10	—	—	—	—	521 (4.1)	796 (4.7)
11	—	—	—	—	1,339 (10.4)	1,749 (10.4)

consistent with recommendations for patients at higher risk of recurrence. Notably, our analysis was performed before the routine availability of Oncotype DX (Genomic

Health, Redwood City, CA, U.S.A.), a test for women with hormone receptor-positive, node-negative disease that identifies patients at low or moderate risk of recurrence, and so interprovincial differences cannot be explained by potential differential access to that test²⁶.

Ontario had the highest proportion of patients experiencing an EDV (36.1%), but the lowest proportion experiencing H (6.4%), similar to proportions in previous reports^{8,17}. Conversely, British Columbia had the lowest proportion of patients experiencing an EDV (16%), but the highest proportion experiencing H (26.7%). Interestingly, the proportion of patients experiencing an EDVH during treatment was very similar in all provinces (13.9%–16.8%). Those observations suggest that there might be interprovincial differences in how acute issues are managed during active cancer treatment, with Ontario patients frequently attending the emergency department for acute issues, while in other provinces, patients are more frequently directly admitted to hospital. Preventing avoidable visits during chemotherapy has been identified as a strategic priority for Cancer Care Ontario²⁷, but other provinces have been less focused on that issue.

A previous Ontario report²⁸ about acute-care use during chemotherapy for bca found that most visits occurred outside of regular business hours (71%) and that, based on triage codes, non-urgent EDVs occurred in higher proportion among patients residing in rural areas than among their urban counterparts (43.5% vs. 14.2%). Likewise, we found rurality to be associated with experiencing an EDV in British Columbia, Manitoba, and Ontario. Geographic location was associated with experiencing either an EDV or H in all provinces. In all provinces, higher comorbidity burden was associated with experiencing an EDV, and in all provinces except Nova Scotia, comorbidities and geographic location were associated with experiencing an EDVH. Those findings suggest that certain patient groups might be at higher risk of having acute-care visits during treatment. Although some patients might require acute care during chemotherapy, high rates of acute care use, when combined with inter- and intraprovincial variation, suggest that some patients might have difficulty accessing care when needed. High rates of unplanned visits by cancer patients, especially during treatment, have been reported beyond Canada^{29,30}, and identifying optimal models of care delivery to this population is an active area of research^{31–33}.

Algorithms to identify chemotherapy-related EDV were previously established⁸ and validated¹⁷ for use with the NACRS database, which captures up to 10 diagnosis codes per visit. However, because complete NACRS data were not available for all provinces, the incidences of EDV and H in the present study were identified using physician billing codes, which capture only 1 diagnosis per visit and might use codes different from those captured by NACRS. The proportion of patients experiencing at least 1 EDV or H related to neutropenia was low compared with previous findings, but similar across provinces (EDV: 0%–1.6%; EDVH: 7.1%–10.1%; H: 0.6–1.9%), suggesting that the algorithm might not perform well when applied to physician billing data.

Our findings must be interpreted within the limitations of the study design. Our study found inter- and intraprovincial variations in treatment and acute care use in

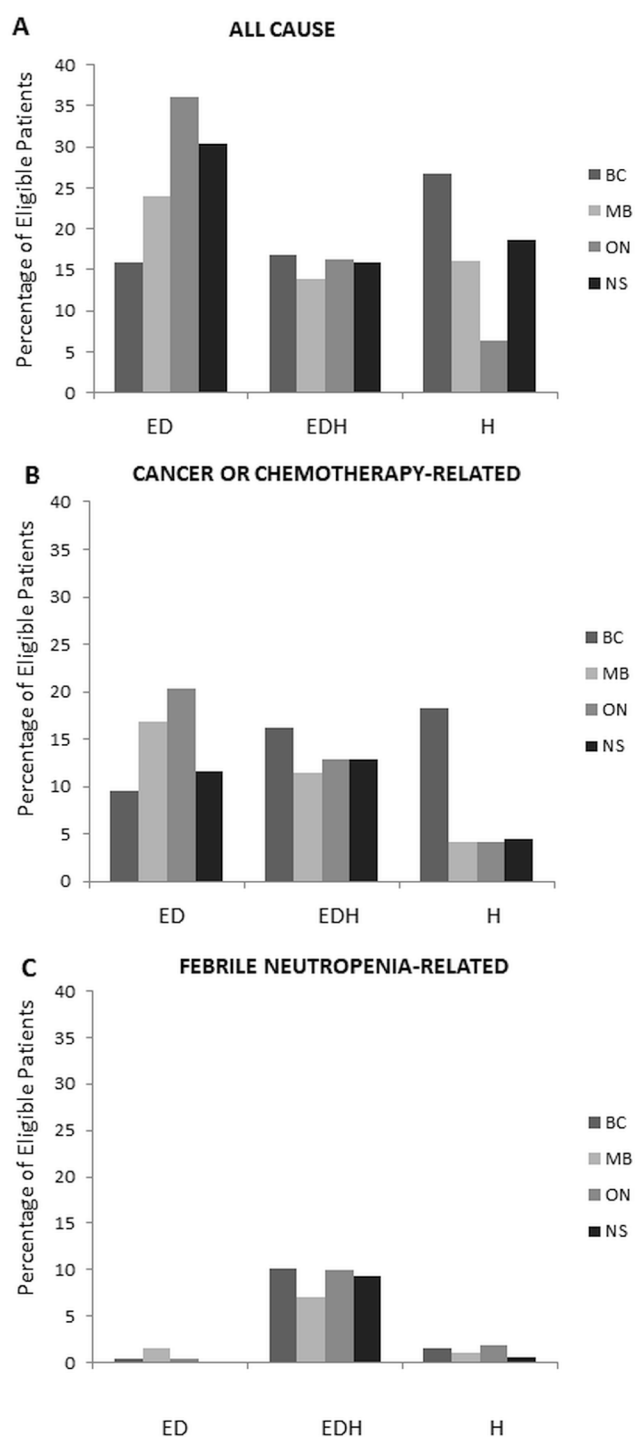


FIGURE 1 For each of four provinces (British Columbia, Manitoba, Nova Scotia, Ontario), the percentage of eligible patients experiencing at least 1 emergency department (ED) visit, 1 ED visit resulting in a hospitalization (EDH), or 1 direct admission to hospital (H). (A) All causes. (B) Cancer- or chemotherapy-related causes. (C) Febrile neutropenia-related.

TABLE III Characteristics of patients treated with adjuvant chemotherapy who experienced at least 1 emergency department visit

Characteristic	British Columbia, 2007–2011 (n=691, 16.0%)		Manitoba, 2007–2012 (n=353, 24.0%)		Ontario, 2007–2011 (n=4646, 36.2%)		Nova Scotia, 2007–2012 (n=345, 30.5%)	
	[n (% ^a)]	Overall p value	[n (% ^a)]	Overall p value	[n (% ^a)]	Overall p value	[n (% ^a)]	Overall p value
Age group								
<40 Years	52 (16.7)	0.22	34 (26.2)	<0.01	519 (40.0)	<0.01	26 (34.2)	0.01
40–49 Years	171 (13.9)		69 (17.0)		1182 (35.8)		107 (32.4)	
50–59 Years	242 (16.5)		135 (26.3)		1438 (33.8)		117 (32.8)	
60–69 Years	184 (17.7)		82 (25.2)		1172(38.3)		78 (29.7)	
70–74 Years	28 (14.3)		21 (30.9)		215 (35.3)		≤15	
>74 Years	14 (17.1)		12 (40.0)		120 (36.5)		≤5	
Income quintile								
Q1 (lowest)	125 (16.2)	0.35	54 (28.3)	0.26	800 (39.4)	<0.01	68 (38.0)	0.03
Q2	134 (16.8)		70 (26.2)		903 (37.5)		60 (27.5)	
Q3	156 (17.6)		70 (24.0)		935 (36.9)		56 (23.8)	
Q4	141 (15.2)		91 (24.1)		1002 (35.3)		82 (31.2)	
Q5 (highest)	126 (14.1)		68 (19.8)		988 (32.8)		79 (33.5)	
Unknown	9 (20.9)		—		18 (43.9)		—	
Deprivation index								
Q5 (most deprived)	NA	NA	70 (29.2)	<0.01	575 (38.8)	<0.01	94 (26.7)	0.02
Q4	NA		90 (32.0)		763 (38.4)		71 (29.3)	
Q3	NA		58 (20.9)		998 (37.2)		74 (41.3)	
Q2	NA		60 (20.2)		1086 (35.5)		59 (31.9)	
Q1 (least deprived)	NA		54 (16.7)		1161 (33.1)		45 (27.0)	
Unknown	NA		21 (39.6)		63 (48.5)		—	
Comorbidities (ADGs)								
0–3 ADGs	195 (12.2)	<0.01	86 (21.2)	<0.01	1079 (30.1)	<0.01	70 (25.7)	<0.01
4–5 ADGs	178 (15.6)		72 (20.8)		1090 (34.9)		72 (27.4)	
6–7 ADGs	132 (16.8)		73 (23.0)		1042 (36.8)		64 (27.8)	
8–9 ADGs	106 (21.7)		52 (25.5)		728 (39.7)		60 (33.2)	
≥10 ADGs	80 (26.5)		70 (35.2)		707 (47.8)		79 (42.3)	
Health authority ^b								
1	202 (25.2)	<0.01	40 (25.3)	<0.01	234 (32.8)	<0.01	18 (30.5)	<0.01
2	277 (18.2)		25 (43.9)		413 (41.1)		17 (25.0)	
3	70 (7.3)		69 (44.0)		222 (33.6)		43 (47.3)	
4	53 (6.7)		78 (43.6)		380 (25.8)		36 (43.4)	
5	88 (38.4)		141 (15.3)		214 (39.4)		≤5	
6	—		—		255 (33.7)		10 (21.3)	
7	—		—		353 (33.0)		≤10	
8	—		—		551 (30.8)		67 (31.6)	
9	—		—		662 (38.6)		145 (28.4)	
10	—		—		276 (53.0)		—	

TABLE III Continued

Characteristic	British Columbia, 2007–2011 (<i>n</i> =691, 16.0%)		Manitoba, 2007–2012 (<i>n</i> =353, 24.0%)		Ontario, 2007–2011 (<i>n</i> =4646, 36.2%)		Nova Scotia, 2007–2012 (<i>n</i> =345, 30.5%)	
	[<i>n</i> (% ^a)]	Overall <i>p</i> value	[<i>n</i> (% ^a)]	Overall <i>p</i> value	[<i>n</i> (% ^a)]	Overall <i>p</i> value	[<i>n</i> (% ^a)]	Overall <i>p</i> value
Health authority ^b continued								
11	—		—		501 (37.4)		—	
12	—		—		225 (43.1)		—	
13	—		—		239 (49.3)		—	
14	—		—		118 (46.3)		—	
Unknown	≤5		—		≤5		—	
Residence								
Urban	506(13.5)	<0.01	176 (16.4)	<0.01	3847 (34.2)	<0.01	258 (32.5)	0.65
Rural	182 (32.7)		177 (44.3)		797 (49.8)		87 (25.7)	
Unknown	≤5		—		≤5		—	

^a With event.^b Used as a proxy for evaluating geographic variation. Number of health authorities vary by province. ADGs = Aggregate Diagnosis Groups (Johns Hopkins, Baltimore, MD, U.S.A.).

the 4 participating provinces. Findings might therefore not be generalizable to other Canadian provinces; however, our study methods could be used to evaluate and compare care in the remaining provinces. Common research and analytic methods were used in each province, but variation in the operationalization of variables and in billing practices across provinces could not be eliminated. Administrative data allow for the evaluation of province-level treatment practices and acute care use, but they lack the additional contextual clinical information, such as access to health care or individual care preferences, that is needed to assess the appropriateness of the care provided. In some cases, for provinces with smaller cohort sizes such as Manitoba and Nova Scotia, results might not be significant because of statistical power issues; in other situations, the statistically significant findings might not be clinically relevant. The proportion of visits considered cancer- or chemotherapy-related was lower than reported in previous studies^{8,17,18}, suggesting that the algorithm might not be suitable for use with physician billing data. Lastly, attribution of visits to specific agents was beyond the scope of our study, and we were also not able to consider acute care use during other systemic adjuvant treatments such as endocrine therapy.

CONCLUSIONS

Intra- and interprovincial differences in the use of chemotherapy and in the incidence of acute care use were observed. Overall, high use of acute care was observed, although treatments and types of acute-care visits differed by province. The observed associations of patient-level demographics and clinical characteristics with experiencing acute-care visits suggests that certain patient groups might be at highest risk. Further research is

required to understand how local care delivery accounts for those differences to identify opportunities for learning and improvement.

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TABLE IV Characteristics of patients treated with adjuvant chemotherapy who experienced at least 1 emergency department visit resulting in a hospital admission

Characteristic	British Columbia, 2007–2011 (<i>n</i> =770, 17.8%)		Manitoba, 2007–2012 (<i>n</i> =205, 13.9%)		Ontario, 2007–2011 (<i>n</i> =2077, 16.2%)		Nova Scotia, 2007–2012 (<i>n</i> =180, 15.9%)	
	[<i>n</i> (% ^a)]	Overall <i>p</i> value	[<i>n</i> (% ^a)]	Overall <i>p</i> value	[<i>n</i> (% ^a)]	Overall <i>p</i> value	[<i>n</i> (% ^a)]	Overall <i>p</i> value
Age group								
<40 Years	50 (16.0)	<0.01	18 (13.9)	0.07	221 (17.0)	<0.01	18 (23.7)	0.26
40–49 Years	185 (15.1)		44 (10.9)		464 (14.1)		46 (13.9)	
50–59 Years	240 (16.4)		67 (13.0)		610 (14.4)		60 (16.8)	
60–69 Years	232 (22.4)		60 (18.5)		559 (18.3)		43 (16.4)	
70–74 Years	37 (18.9)		≤15		143 (23.4)		≤10	
>74 Years	26 (31.7)		≤5		80 (24.3)		≤5	
Income quintile								
Q1 (lowest)	141 (18.3)	0.47	35 (18.3)	0.41	358 (17.6)	0.37	30 (16.8)	0.46
Q2	152 (19.0)		38 (14.2)		371 (15.5)		29 (13.3)	
Q3	165 (18.6)		35 (12.0)		402 (15.9)		36 (15.3)	
Q4	166 (17.9)		54 (14.3)		453 (16.0)		49 (18.6)	
Q5 (highest)	138 (15.5)		43 (12.5)		483 (16.0)		35 (14.8)	
Unknown	8 (18.6)		—		10 (24.4)		≤5	
Deprivation index								
Q5 (most deprived)	NA	NA	34 (14.2)	<0.01	245 (16.5)	0.55	55 (15.6)	0.91
Q4	NA		38 (13.5)		336 (16.9)		36 (14.9)	
Q3	NA		43 (15.5)		433 (16.1)		33 (18.4)	
Q2	NA		29 (9.8)		504 (16.5)		31 (16.8)	
Q1 (least deprived)	NA		45 (13.9)		537 (15.3)		24 (14.4)	
Unknown	NA		16 (30.2)		22 (16.9)		—	
Comorbidities								
0–3 ADGs	229 (14.3)	<0.01	40 (9.9)	<0.01	469 (13.1)	<0.01	36 (13.2)	0.38
4–5 ADGs	204 (17.8)		39 (11.3)		465 (14.9)		38 (14.5)	
6–7 ADGs	140 (17.9)		40 (12.6)		483 (17.1)		37 (16.1)	
8–9 ADGs	117 (24.0)		46 (22.6)		336 (18.4)		33 (18.2)	
≥10 ADGs	80 (26.5)		40 (20.1)		324 (21.9)		36 (19.2)	
Health authority ^b								
1	170 (21.2)	<0.01	22 (13.9)	<0.01	90 (12.6)	<0.01	10 (17.0)	0.14
2	335 (22.0)		10 (17.5)		158 (15.7)		10 (14.7)	
3	109 (11.4)		30 (19.1)		67 (10.2)		19 (20.9)	
4	106 (13.5)		37 (20.7)		201 (13.6)		15 (18.1)	
5	49 (21.4)		106 (11.5)		109 (20.1)		≤5	
6	—		—		119 (15.7)		11 (23.4)	
7	—		—		180 (16.8)		≤10	
8	—		—		311 (17.4)		23 (10.9)	
9	—		—		300 (17.5)		81 (15.9)	
10	—		—		104 (20.0)		—	

TABLE IV Continued

Characteristic	British Columbia, 2007–2011 (n=770, 17.8%)		Manitoba, 2007–2012 (n=205, 13.9%)		Ontario, 2007–2011 (n=2077, 16.2%)		Nova Scotia, 2007–2012 (n=180, 15.9%)	
	[n (% ^a)]	Overall p value	[n (% ^a)]	Overall p value	[n (% ^a)]	Overall p value	[n (% ^a)]	Overall p value
Health authority ^b continued								
11	—		—		198 (14.8)		—	
12	—		—		74 (14.2)		—	
13	—		—		78 (16.1)		—	
14	—		—		87 (34.1)		—	
Unknown	≤5		—		≤5		—	—
Rurality								
Urban	666 (17.7)	0.71	126 (11.8)	<0.01	1794 (16.0)	0.10	122 (15.4)	0.44
Rural	102 (18.3)		79 (19.8)		282 (17.6)		58 (17.2)	
Unknown	≤5		—		≤5		—	

^a With event.^b Used as a proxy for evaluating geographic variation. Number of health authorities vary by province. ADGs = Aggregate Diagnosis Groups (Johns Hopkins, Baltimore, MD, U.S.A.).

Data for this study were also provided by Population Data BC and BC Cancer. All inferences, opinions, and conclusions drawn in this study are those of the authors, and do not reflect the opinions or policies of the B.C. Data Steward(s) [BC Cancer Registry; Population Data BC, Vital Statistics, Deaths; Population Data BC, Medical Services Plan Payment Information File (<http://www.popdata.bc.ca/data>).

This study was approved by the University of Manitoba's Health Research Ethics Board and Manitoba Health's Health Information and Privacy Committee. We gratefully acknowledge CancerCare Manitoba for their ongoing support and Manitoba Health for the provision of data. The results and conclusions presented are those of the authors. No official endorsement by Manitoba Health is intended or should be inferred.

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CONFLICT OF INTEREST DISCLOSURES

We have read and understood *Current Oncology's* policy on disclosing conflicts of interest, and we declare that we have none.

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TABLE V Characteristics of patients treated with adjuvant chemotherapy that experienced at least one direct hospital admission (H) by province

Characteristic	British Columbia, 2007–2011 (<i>n</i> =1155, 26.7%)		Manitoba, 2007–2012 (<i>n</i> =237, 16.1%)		Ontario, 2007–2011 (<i>n</i> =828, 6.4%)		Nova Scotia, 2007–2012 (<i>n</i> =211, 18.6%)	
	[<i>n</i> (% ^a)]	Overall <i>p</i> value	[<i>n</i> (% ^a)]	Overall <i>p</i> value	[<i>n</i> (% ^a)]	Overall <i>p</i> value	[<i>n</i> (% ^a)]	Overall <i>p</i> value
Age group								
<40 Years	122 (39.1)	<0.01	33 (25.4)	0.04	107 (8.2)	0.01	27 (35.5)	<0.01
40–49 Years	347 (28.3)		55 (13.6)		217 (6.6)		67 (20.3)	
50–59 Years	365 (24.9)		77 (15.0)		256 (6.0)		63 (17.7)	
60–69 Years	256 (24.7)		56 (17.2)		173 (5.7)		35 (13.3)	
70–74 Years	42 (21.4)		≤15		51 (8.4)		8 (15.1)	
>74 Years	23 (28.0)		≤5		24 (7.3)		11 (20.4)	
Income quintile								
Q1 (lowest)	200 (26.0)	0.35	37 (19.4)	0.54	144 (7.1)	0.60	38 (21.2)	0.48
Q2	194 (24.3)		49 (18.4)		141 (5.9)		35 (16.1)	
Q3	245 (27.7)		44 (15.1)		160 (6.3)		37 (15.7)	
Q4	266 (28.6)		56 (14.9)		186 (6.6)		55 (20.9)	
Q5 (highest)	236 (26.5)		51 (14.9)		194 (6.4)		46 (19.5)	
Unknown	14 (32.6)		—		≤5		—	
Deprivation index								
Q5 (most deprived)	NA	NA	51 (21.3)	0.07	112 (7.6)	0.01	86 (24.4)	0.01
Q4	NA		48 (17.1)		142 (7.2)		38 (15.7)	
Q3	NA		39 (14.1)		135 (5.0)		22 (12.3)	
Q2	NA		46 (15.5)		203 (6.6)		30 (16.2)	
Q1 (least deprived)	NA		41 (12.7)		231 (6.6)		34 (20.4)	
Unknown	NA		12 (22.6)		≤5		—	
Comorbidities								
0–3 ADGs	400 (25.0)	0.09	59 (14.5)	0.03	227 (6.3)	0.79	45 (16.5)	0.37
4–5 ADGs	299 (26.2)		43 (12.4)		192 (6.1)		46 (17.5)	
6–7 ADGs	220 (28.1)		54 (17.0)		183 (6.5)		39 (17.0)	
8–9 ADGs	151 (30.9)		46 (22.6)		121 (6.6)		39 (21.6)	
≥10 ADGs	85 (28.4)		35 (17.6)		105 (7.1)		42 (22.5)	
Health authority ^b								
1	214 (26.7)	<0.01	29 (18.4)	<0.01	51 (7.2)	<0.01	6 (10.2)	0.04
2	460 (30.2)		13 (22.8)		125 (12.4)		10 (14.7)	
3	286 (29.8)		37 (23.6)		48 (7.3)		11 (12.1)	
4	140 (17.8)		37 (20.7)		95 (6.5)		14 (16.9)	
5	52 (22.7)		121 (13.1)		27 (5.0)		≤5	
6	—		—		40 (5.3)		≤10	
7	—		—		75 (7.0)		15 (26.3)	
8	—		—		92 (5.1)		56 (26.4)	
9	—		—		83 (4.8)		89 (17.5)	
10	—		—		24 (4.6)		—	

TABLE V Continued

Characteristic	British Columbia, 2007–2011 (n=1155, 26.7%)		Manitoba, 2007–2012 (n=237, 16.1%)		Ontario, 2007–2011 (n=828, 6.4%)		Nova Scotia, 2007–2012 (n=211, 18.6%)	
	[n (% ^a)]	Overall p value	[n (% ^a)]	Overall p value	[n (% ^a)]	Overall p value	[n (% ^a)]	Overall p value
Health authority ^b continued								
11	—		—		94 (7.0)		—	
12	—		—		20 (3.8)		—	
13	—		—		24 (5.0)		—	
14	—		—		30 (11.8)		—	
Unknown	≤5		—		—		—	
Residence								
Urban	1,020 (27.2)	0.15	151 (14.1)	<0.01	732 (6.5)	0.69	146 (18.4)	0.73
Rural	132 (23.7)		86 (21.5)		96 (6.0)		65 (19.2)	
Unknown	≤5		—		—		—	

^a With event.^b Used as a proxy for evaluating geographic variation. Number of health authorities vary by province. ADGs = Aggregate Diagnosis Groups (Johns Hopkins, Baltimore, MD, U.S.A.).

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